UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,363	12/11/2001	Josef Burg	20805	1126

151 7590 12/03/2004

HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER	
SCHNIZER, HOLLY G	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,363	BURG ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18-20,22 and 23* is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *21,24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/02 &11/25/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-25 are pending and have been considered in this Office Action.

Specification

The Specification is objected to for failing to comply with the sequence rules. The Drawings contain sequences without sequence identifiers (including in the Brief Description of the Drawings. Where the description of a patent application discusses a sequence of 4 or more amino acids, reference must be made to the sequence by use of the sequence identifier preceded by "SEQ ID NO:" in the text of the description even if the sequence is also embedded in the text of the description of the patent application (see 37 C.F.R. 1.821, especially paragraphs (a)-(d)). The sequence identifier may be used in either the drawing or the Brief Description of Drawings (see MPEP 2429, helpful hint no. 21). Correction is required.

Claim Objections

Claims 10, 21, 24, and 25 are objected to because they refer to sequences by figure number rather than by sequence identifier (SEQ ID NO:). Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a

necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted) (see MPEP2173.05(s)). In the instant case, the sequences should be referred to by their sequence identifier. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 5, and 7 are unclear as to the metes and bounds of "about". The symbol "m" represents the number of repeats within the given formula (how many repeats of (OCH_2CH_2)). . The claims are unclear as to how many additional repeats are encompassed by "about" and whether or not "about" represents a repeat of a fractional portion of (OCH_2CH_2). The specification fails to define how many repeats are encompassed by the term "about". Therefore, the metes and bounds of the claims are unclear. Claim 6 is rejected because it depends from rejected claim 4 yet does not correct its deficiencies. Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-17 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,583,272 (the '272 patent).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The '272 patent teaches and claims a conjugate comprising an erythropoietin (EPO) glycoprotein having an N-terminal alpha amino group and one poly(ethyleneglycol) (PEG) wherein the EPO glycoprotein can be human EPO, analogs thereof with 1 to 6 additional sites for glycosylation, or human EPO with at least one glycosylation site that is rearranged and wherein the glycoprotein is covalently linked to the PEG group of a formula identical to that of claim 1 of the present invention including the values of m, x, and R (see claims of '272 patent). The '272 patent teaches that "m"

of the formula disclosed therein can be 450 to 900 which is within the range taught in the presently claimed invention. The '272 patent teaches that the glycoprotein can be expressed by endogenous gene activation (see clm. 4 of '272 patent) and that the glycoprotein has a sequence identical to that shown in Figure 1 of the present Specification (SEQ ID NO:1 of the '272 patent). The '272 patent teaches that the EPO glycoprotein of the conjugate may be modified by the addition of from 1 to 6 glycosylation sites (clm. 10 of '272 patent) and may be modified by a modification identical to claim 12 of the present application (see clm. 11 of the '272 patent). The '272 patent teaches that the glycoprotein may be modified by a rearrangement of at least one glycosylation site (clm. 12 of '272 patent) or more specifically by deletion of any of the N-linked glycosylation sites and addition of an N-linked glycosylation site at position 88 of the sequence of human EPO (see clm. 13 of '272 patent) including any modifications of present claim 15 (see claim 14 of '272 patent). The '272 patent teaches that the EPO conjugate can be placed in a pharmaceutical composition including a pharmaceutically acceptable excipient (Col. 7, lines 8-23; Col. 3, lines 33-45). The '272 patent indicates that the EPO conjugates disclosed therein may be used in therapeutic methods in the same manner as unmodified EPO (Col. 3, lines 7-8) such as methods of treating anemia in chronic renal failure patients, AIDS, and cancer patients undergoing chemotherapy (Col. 1, lines 42-55).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 10-14 of U.S. Patent No. 6,583,272. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g. In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because Claims 1-15 are generic to all that is recited in claims 1-6 and 10-14 of U.S. Patent No. 6,583,272. That is, claims 1-6 and 10-14 of U.S. Patent No. 6,583,272 fall entirely within the scope of Claims 1-6 and 8-15, or in other words, Claims 1-6 and 8-15 are anticipated by Claims 1-6 and 10-14 of U.S. Patent No. 6,583,272. Specifically, the EPO conjugates of claims 1, 2, 4, 5, and 8-9 have identical EPO moiety and identical structure of the PEG moiety as claims 1-4 of U.S. Patent No. 6,583,272 except that m has a wider range. Moreover, it would be inherent that the claimed

conjugates of claims 1, 2, 4, 5, and 8-9 would have the same activity as the identical conjugates of claims 1-4 of the patent and the 'm' values of the patent are within the 'm' values of claims 1, 4, and 5 of the present application. The conjugate of Claim 6 of the patent is the compound of claim 3 of the present application when the glycoprotein is human EPO of Figure 1. The conjugate of claim 3 of the patent is the compound of claim 6 of the present application when R is methyl and the compound of claim 8 of the present application. The sequence of figure 1 as claimed in claim 10 of the present application is identical to the sequence of SEQ ID NO:1 of claim 5 of the patent. In addition, the glycosylation patterns claimed in claims 10-14 of the patent are identical to those claimed in claims 11-15 of the present application. In addition, the conjugate of claim 2 of the patent is the conjugate of claim 7 of the present application when R is a methyl.

Claim 16 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,583,272.

An obviousness type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim because the examined claim is either anticipated by or would have been obvious over the reference claim. See, In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, claim 1 of the patent recites EPO conjugates that are fully encompassed by the conjugates contained in the composition of claim 16 of the present application.

Claim 16 differs from claim 1 of the patent in that it discloses a pharmaceutical composition comprising the EPO conjugate and a pharmaceutically acceptable excipient. However, the portion of U.S. Patent No. 6,583,272 that supports the utility of the conjugates disclosed therein teaches that the conjugates may be formulated into pharmaceutical compositions containing the conjugate and a pharmaceutically acceptable excipient for treatment of anemia in the same manner as routine treatments using unmodified EPO (see Col. 2, lines 24-27, Col. 3, lines 7-10 and lines 32-35). Therefore, it would have been obvious to place the disclosed conjugates of the patent into a pharmaceutical composition to use in treating anemia as is routine for unmodified EPO. One having ordinary skill in the art would have been motivated to make such a pharmaceutical composition since the disclosed conjugates have an increased half-life and plasma residence time.

Conclusions

Claims 1-17 are rejected. Claims 10, 21, 24, and 25 are objected to. Claims 18-20 and 22-23 are in condition for allowance. Claims 18-25 are free of the prior art. A thorough search of the prior art did not reveal any teaching or suggestions of a method of making the conjugates of the invention using a recombinant EPO that has an N-terminal peptidic extension and following the specific steps of present claims 18-25.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-

0958. The examiner can normally be reached on Monday through Wednesday from 8 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Holly Schnizer
November 22, 2004

JON WEBER
SUPERVISORY PATENT EXAMINER